Great Lakes Positive Handbook

'A Guide to Antiretroviral Therapy - (ARV)'
Issue 1 (Jan 2005)

Community Health And
Information Network (CHAIN)
www.chainproject.org

HIV i-base
www.i-base.info

Contents

Forward

With HIV/AIDS drugs becoming more accessible especially through National Antiretroviral Therapy (ART)Programmes in the Great Lakes countries (Uganda, Kenya, Rwanda, Tanzania, Burundi & Democratic Republic of Congo), there is an urgent need to empower people on medication so that they can adhere effectively on their medications and avoid HIV resistance. This publication aims to do exactly that. CHAIN in partnership with EANNASO and the Burundi National Network of People Living With HIV / AIDS will be launching this booklet at the Treatment Literacy / Capacity Building Workshop organised by the three partners. This workshop will take place in Bujumbura, Burundi between 13th - 15th December 2004.

Its evident that treatment literacy is still very much lacking in the above mentioned countries. Community Health And Information Network (CHAIN) in partnership with HIV i-Base in London and all key stakeholders in the region have come together to produce this publication. This has been informed by the treatment needs which were identified from the treatment empowerment workshops we held in the above countries over the past two years.

With the help of our partners and policy makers within the Great Lakes Region, we hope to produce this publication once a year and also translate it in various languages. The booklet will initially be available in English and French.

We MUST emphasise that this publication does not negate the treatment publications which might be already available in these countries. The publication aims to compliment what might be already available.

The publication is targeting all people on medication or those thinking of starting medication, doctors, clinicians, nurses and midwives who are treating patients, health care workers, Community Based Organisations (CBOs) supporting people on medication and policy makers.

Let me take this opportunity to thank Simon Collins – Treatment Editor – HIV i-Base, Dr Chris Wood, HIV Consultant at North Middlesex Hospital, London, all CHAIN volunteers and all our funders for making this publication possible. We look forward to continue working with you and also get more partners on board. Special thanks to Dr Anthony Kebba & Dr Lydia Mungerera who have accepted to join the editorial board. ***We shall be finalising our editorial board by the end of December 2004.***

Being that this is the first edition, we are keen to have your comments and suggestions so that we could ensure that information produced meets your needs. There is a feedback form at the end of this publication which I kindly request you to fill and return to our Treatments Editor based at our office in Uganda.

Yours sincerely

William Babumba
***Chair* - CHAIN**

Introduction to this guide

Getting as much information as possible before you start therapy is very important. It will help you make informed decisions about your treatment.

Information about HIV treatment changes very quickly. So only rely on information, whether printed or from the internet, that is clearly dated and that is up to date. This booklet was accurate in 2004.

If you are only learning about HIV for the first time, then discuss any question with your friends and family who know you are HIV-positive, or with your doctors or healthcare workers.

This handbook is written by HIV-positive people who are already on treatment, CHAIN Trained Treatment Advocates and doctors prescribing ARVs. It refers to the latest WHO treatment guidelines but also comments on how HIV is treated in different countries. These guidelines are a good reference for a minimum standard of care and should be updated every year.

The following guidelines are available on the internet:

WHO:	http://www.who.int/3by5/publications/documents/arv_guidelines/en/
UK:	http://www.bhiva.org
US:	http://www.aidsinfo.nih.gov

“getting as much information as possible before you start therapy is very important”

Information in this booklet is not intended to replace information from your doctor or other healthcare workers. Decisions relating to your treatment should always be taken in consultation with your doctor.

What, why, when & other questions...

Starting treatment

This booklet may be the first information that you have read about HIV treatment. You may only just have found out that you are HIV-positive, so this can also be a difficult time - but it will get easier.

You may want to read this handbook now in one go, or come back to read different sections later, but the information is important.

Although many of the terms used may be new, if you understand how the treatment works you should have a better chance that the drugs will work.

What is combination therapy?

Combination therapy is the term for using three or more drugs to treat HIV. It is also called triple therapy or HAART (Highly Active Anti-Retroviral Therapy).

The treatment only works because there are three different drugs all fighting the virus. If you miss doses or are late then taking them, then they may not work at all, or will only work for a few months. HIV is a difficult disease to treat,

Do the drugs really work?

Yes! In every country that uses HAART, AIDS-related deaths and illnesses drop dramatically.

Treatment works for women, men and children. It works no matter how you were infected with HIV. Whether this was sexually, through IV drug use, or by blood transfusion.

Taking HIV drugs, exactly as prescribed, will reduce the virus in your body to tiny amounts. This then lets your immune system recover and get stronger by itself.

Now that there are treatments for HIV, this is an important reason to know whether you are HIV-positive.

The CD4 test

The test that measures how strong your immune system is, and how much damage has been cause by HIV, is called a CD4 or T4 test.

After infection, your CD4 count falls and then recovers. It then falls again more slowly (usually over several years). A count of 200 is a guide to start treatment.

Your CD4 count should rise again above 200 if your treatment is working.

Even though it is important for general monitoring, this test is mainly used to decide when you need to start treatment. If you have any HIV-related illnesses then you may need treatment even at a higher CD4 count.

If you do not have access to regular CD4 tests, you can still benefit from treatment. It is even more important that you take every dose of treatment exactly as it is prescribed.

Even if you start with a very low CD4 count below 50, you could regain enough of your own immune system for your body to recover from many HIV-related illnesses.

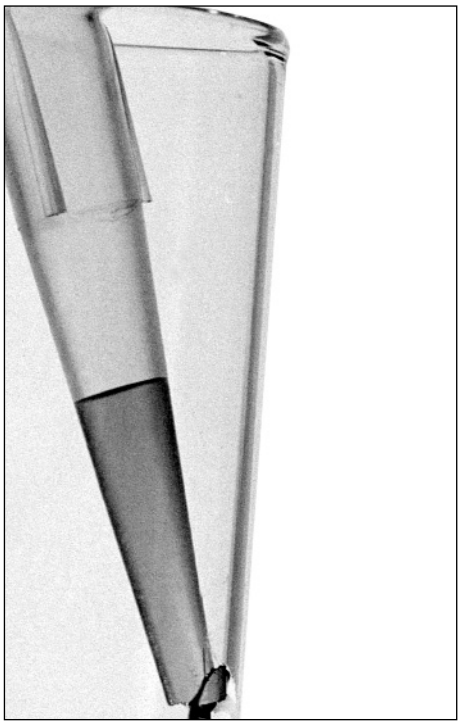
If you use HIV treatment at the right time, and in the right way, you should stay well for a long time.

What is a viral load test

A viral load test measure how much HIV is in a sample of blood.

After infection, viral load levels are very high, and then your body fights back and brings the levels down much lower. Over time though the levels of virus increases again, it is usually very high by the time that your CD4 count reaches 200.

The viral load test is used after you start treatment to check that the drugs are working. If viral load is brought down to less than 50 copies/mL then treatment will last for a long time.



These tests are used in many countries but are difficult to get in many others. In some countries, the tests cost much more than the drugs. New research is also looking at developing new tests that will be just as good but which are not so expensive or difficult to run.

Even if you don not have access to these test, it makes a difference that you understand how CD4 and viral load change.

These two tests tell any doctor 95% of what they need to know about your health and your treatment.

How long will the drugs work?

Combination therapy using three drugs has now been used in some countries for over eight years. Many of the individual drugs have been studied for even longer.

The length of time that any combination will work depends mainly on you not developing resistance. This depends on getting, and keeping, your viral load to undetectable levels, below 50 copies/mL.

If your viral load stays undetectable, you can use the same combination for years.

Does everyone need treatment?

At some point, nearly all HIV-positive people will need treatment. When people will need it though, can vary a lot. HIV infection progresses in different people at very different rates.

- About one third of HIV-positive people will stay well for up to 10 years after infection, even without treatment.
- About 60% will need to start treatment after 4-5 years.

- 2-3% of people become ill more quickly and need treatment much earlier.

- 2-3% can go for 15-20 years without treatment.

Whether you need treatment is something you have to discuss with your doctor. This will usually take place over several visits. In most countries treatment is not free and its very important that a patient makes the decision having assessed their financial profile. Some countries have subsidized these drugs which will make them more accessible and affordable in years to come.

When discussing treatment:

- Ask as many questions as possible until you are happy with the answers.

- Get useful information from other sources. This includes; Ministry of Health (MOH), friends, health workers, support groups, newsletters,Non Government Organisations (NGOs), Community Based Organisations (CBOs), Faith Based Organisations (FBOs), phone lines and the internet.

Even if you are well, it is a good idea to get to know something about treatment now, before you need it.

This is important if your CD4 count is falling, or if you have a high viral load.

When to start treatment

When to start treatment is something you and your doctor must discuss together. You are the person who has to take the pills. So, you have the choice over whether you start, as well as which drugs you use.

It is recommended to start treatment before your CD4 count falls below 200. Even at this level, there is unlikely to be an urgent need for you to start treatment straight away, if you are not ready.

- Ask your doctor to tell you about the different drugs that you can use. You need to know the good and bad things about each of them.

- Take time to think about what you want to do. Do not feel rushed or pressured into doing something you don't understand. If you have only recently been diagnosed HIV-positive, you will need to deal with that first.

While your CD4 count is above 300, you still have a good immune system. Below 300 you are at a higher risk of infections that cause diarrhoea and weight loss.

"ask as many questions as possible until you are happy with the answers"

If your CD4 count falls below 200, your risk of developing a pneumonia called PCP increases. If it falls below 100, then your risk of serious illnesses increases even further.

A low CD4 count does not mean that you will definitely become ill. It is, however, much more likely. Most of the drugs used to treat these HIV-related illnesses can be more toxic and difficult to take than regular anti-HIV drugs.

Although you may be worried about using treatments, HIV and AIDS is a very real and life-threatening illness. Illnesses that can occur at any time when your CD4 count is below 200 can be fatal.

Is treatment the same for people with TB?

TB (and malaria) can be harder to treat if you also have HIV. They can also make HIV progress more quickly. It is very common for people to have more than one infection and it is important for your doctor to know about this.

HIV treatment is recommended for anyone who also has active TB infection, even if the CD4 count is higher than 200. Different HIV drugs are recommended if you also need to take treatment for TB.

Efavirenz should not be used in pregnant woman or in women who may become pregnant. Children with low weight are recommended to use abacavir + 2 RTIs.

Are recommendations the same for men and women?

There are some differences between HIV in women and men. One of these is that at the same CD4 count, women can have a slightly lower viral load than men. Some studies also show that women have a higher risk of becoming ill than men at the same CD4 count but evidence to support this was not strong enough for this to be included in treatment guidelines.

One important difference is that women should not use the drug nevirapine if their CD4 count is over 250 when they start treatment.

What about treatment in pregnancy?

Women with HIV can be effectively treated during pregnancy.

How HIV Treatment differs for those with TB

HIV only	HIV & TB
nevirapine +2 RTIs	efavirenz + 2 RTIs abacavir + 2 RTIs saquinavir + ritonavir + RTIs

Using combination treatment during pregnancy can be better for the mothers health. It can also dramatically reduce the risk of HIV being passed to the baby.

Different guidelines and approaches are used for pregnancy in different countries. Please consult your respective doctor.

For example in some countries, women will be offered one single dose of nevirapine just before they give birth. This can reduce the chance of the baby being HIV-positive, but can also lead to the mother becoming resistant to nevirapine. Using additional drugs during the last weeks of pregnancy can be much better for both the mother and her baby, but it is taking time for these policies to change.

It would be ideal for all HIV-positive women to be able to use a triple combination for at least the last weeks of the pregnancy. This protects the mother from resistance and reduces the risk of the baby being HIV-positive to virtually zero.

Even using AZT+3TC for either 4 or 7 days (starting wit the single nevirapine dose) can significantly reduce the risk of the mother developing resistance.

For more information on HIV and pregnancy, see the leaflet 'HIV, Pregnancy and Women's Health'. **[Please refer to http://www.i-Base.info]**

How do children use HIV treatment?

The principles for treating children with HIV are very similar to those for treating adults. However, there are some important differences.

The immune system and drug absorption can be different in babies, toddlers, infants, children, adolescents and adults. This is why specialist HIV care is recommended at all ages.

" using combination treatment during pregnancy can be better for the mothers health "

For this reason, there are separate treatment guidelines for treating children. However, they tend to be updated less frequently than adult guidelines. It is therefore important to be aware of changes in adult care that may be just as relevant for children.

Adherence is the term for taking all your medications exactly as prescribed. This is essential at any age. Resistance can develop regardless of age if you use a treatment that does not get your viral load to undetectable levels.

For more information about children and HIV visit the Children with HIV Association (CHIVA) website: http://www.bhiva.org/chiva

Is age an important factor in adults?

Ageing itself suppresses our immune systems. People over 50 have an increased risk of damage caused by HIV. The argument for starting treatment becomes stronger as you get older.

Treatment guidelines do not yet comment on this apart from in reference to heart disease.

Age, HIV drugs and heart disease

Risk factors for heart disease include age (over 45 for men and over 55 for women), sex (male), lack of exercise, family history of heart disease, high blood pressure, smoking and diabetes.

> *“ if you follow your treatment very carefully, you have a very good chance that the treatment will work ”*

Other risk factors associated with heart disease include raised levels of cholesterol and triglycerides, which can result from eating a high fat diet but can also be a side effect of HIV treatment.

Although the benefits of HIV treatment far outweigh the additional risks of heart disease for most people, this may not be true for everyone. The additional risks that HIV treatment may generate, means that an assessment of cardiovascular and HIV risk factors should be made before starting HIV treatment.

Early diagnosis and primary infection

Some studies are looking at whether there is a benefit from treating people who discover that they are HIV-positive within six months of being infected. This is regardless of their CD4 but the results have not shown any additional benefit.

This option is only available in a few clinical trials.

Unless you have very serious symptoms, you will not normally use HIV treatment until your CD4 count falls to below 200.

Late HIV diagnosis and low CD4s

Some people, from all age ranges, only find out they are HIV-positive when they become ill and admitted to hospital. This often means starting treatment straight away, especially when the CD4 count is below 100.

For people who only discovered they are HIV-positive when their CD4 count is very low, there is still very good news.

Even with a very low CD4 count, even below 10, if you follow your treatment very carefully, you have

a very good chance that the treatment will work. Your viral load will drop and your CD4 count will rise again to safer levels.

What does 'treatment naive' mean?

The term for someone who has never used any anti-HIV drugs before is 'treatment-naive' or 'drug-naive'. This is a very special situation. It means that any of the available drugs should work.

The first time you use anti-HIV drugs is the time they are most potent. This is why it is best to get it right first time.

Should I enter a trial?

Some hospitals are also research centres and you may be asked to join a study.

Studies can offer better monitoring and care than you would normally receive at your regular clinic. This may mean attending your clinic more frequently.

If asked to join a trial, or if you are interested in a trial, take time to think about it. Ask for independent advice. Women should ask the percentage of women that are included in the study.

Trials are very important for developing new treatments. They can improve our knowledge of how to use both new and existing drugs. However, you should not feel pressurised into taking part.

Ask about the alternatives to the treatment proposed in the study. Ask what advantages the study offers over existing treatment.

Your future care will not be affected if you choose not to join a trial.

What else do I need to know?

Ongoing research means that ideas about how to use anti-HIV drugs are changing. The treatment your doctor will use today is likely to be different from a year ago.

Access to new drugs and alternative drugs is also changing and will continue to change in the next few years.

This isn't just because there are newer drugs available. It is to do with understanding how the drugs work, why they sometimes stop working, and especially increasing knowledge about resistance.

Ask questions about anything you don't understand. You can then take responsibility for whatever you decide.

Why do treatments not always work?

For some people the treatments will not work as well. There are several reasons why and these include:

- The combination may not be potent enough – this is why three rather than two drugs are recommended in a combination
- You may already be resistant to one or more of the drugs in your combination.
- You may not have taken every dose at the right time Even if you are only missing one dose a week, it can be enough to make the combination fail.
- One or more of the drugs may not be absorbed properly. There can be big variations between people but it is difficult to test for this.
- Side effects may be too difficult to tolerate.

Trial results never show a 100% success rate. BUT if you have a good doctor, and you follow your regimen carefully, anyone starting treatment for the first time should be able to get an undetectable viral load.

"ask questions about anything you don't understand. You can then take responsibility for whatever you decide"

Success rates for people on their second or third therapy are usually lower than for those starting treatments for the first time.

This is often because people continue to make the same mistakes and move to a new combination without understanding why the original one failed.

This booklet concentrates mainly on the effect of treatment on viral load and CD4 results. *This is because these are the main markers that doctors use to decide if a treatment is working*. Some people may never reach undetectable levels but still stay well and healthy for many years. There are always more responses to treatment than can be summarised here.

You may not get an undetectable viral load, perhaps because of resistance.

However, you can still benefit from continuing treatment. You could also benefit from new drugs that become available in the future

If you need new drugs in order to put together a new combination then make sure you and your doctor keep up-to-date on the latest research.

Are the drugs a cure?

The current drugs are a treatment but not a cure. They can stop the progression of HIV. They let your immune system start to repair itself, but you will still be HIV-positive and are still able to pass HIV to another person.

Even people taking combination therapy for many years, with a viral load below 50 copies/mL still have very small amounts of HIV.

The drugs are getting us closer to finding a cure. You may need medication for a long time, but newer drugs may be easier to take and more effective.

This means you may still get to die of old age rather than from HIV. It may also mean that you are still alive when we find a cure - and this gives us hope.

Don't look at the drugs you start with now as a treatment that you will be taking forever. Look at them as something you have to be really committed to for the next couple of years.

Take this new aspect of your life more seriously than anything else does until you get it right.

You and your doctor

It is essential to develop a good working relationship with your doctor and other specialized healthcare workers and Community Based Organisations providing treatment support services.

Doctors are not the only people at your clinic who are able to help. Nurses and pharmacists are an excellent source of support and advice on all aspects of your treatment.

Your rights as a patient...

- To have different options for treatment explained to you. This should include the risks and benefits of each option.
- To be fully involved in all decisions about your treatment and care.
- To be treated with respect and confidentiality.
- For your records to be kept securely. They should be available for you to see if you ask.
- To choose whether to take part in research trials. This will not affect your current and future care.
- To make a complaint about your treatment. Any complaint must be fully investigated. Again, this must not affect your future care.

Things you can do to help...

- Find a doctor who you feel comfortable with. *This could be difficult in some countries but its important that a patient assesses a number of doctors before making a decision*. If you are a woman and want to see a female doctor then ask for this.
- Make a list of things you want to discuss with your doctor. Remember to take it to your appointment!
- Try to see the same doctor at each visit. This is important. It's difficult to develop a good relationship if you always see a different doctor.
- Turn up for your appointments on time. Tell the clinic or treatment centre if you can't make it. Then they can give your slot to another patient.
- Treat all people involved in your care with the same respect you would wish to receive yourself.
- Listen carefully to the health advice that you are given, and act upon it.
- If you don't understand something, ask your doctor to explain it again or in a different way.
- Be honest with those caring for you. Tell them about any other drugs that you are taking. This includes legal and illegal drugs or complementary treatment.
- Be honest about your level of adherence. If those managing your care don't know you are having problems, they can't help.

Adherence – and why it is so important

What is adherence?

Adherence is a word to describe taking your drugs exactly as they are prescribed. This includes taking them at the right time. It also includes following any special diet restrictions.

This is because HIV drugs will only work if you keep a constant minimum level of each drug in your body all the time. If it drops below this level then your virus can develop resistance to the drugs, and the drugs will stop working.

A little HIV medication is a very dangerous thing. With HIV, you need to take all or nothing. HIV drugs are a bit like TB drugs – you need to take all of them at the right time and continue to take them.

It is important that you develop a routine - even if you only have to take one pill twice a day. You may need some support to get used to the changes it makes in your life. Adherence can be very difficult.

This is the most important thing you have to think about when you start taking a new combination.

Start treatment when you can give yourself the extra time and space you may need to adjust.

During the first few weeks, nothing else should take priority over getting your treatment right.

Your treatment centres may have an adherence clinic or an adherence nurse that can help.

How much is enough?

Taking medication exactly on time is very important. However, there is usually a window period of about an hour that is still okay. Some drugs have a wider window period than others.

Because of this variation, it is still better to aim for the same time each day.

Diet restrictions are very important. Ignoring these can be like only taking half a dose. You will not absorb enough of the drug for it to work properly. Resistance is then more likely to occur which means you loose the chance to use these drugs in the future.

The next question is: 'exactly how close to perfect adherence do you have to get?' Unfortunately, the answer is 'almost 100%'...

Many studies have shown that even missing one or two doses a week can have a big impact on the chances of a successful treatment. On the other hand, a study of people in prison who took every dose showed much better results.

Because these patients were in prison, every dose was supervised. All had viral loads below 400 copies/ml after a year and 85% were below 50 copies/ml.

The point is not that you need to be in prison! It is that if you find a way to take all your drugs as prescribed, you will get good results.

- Be strict with yourself in assessing how adherent you are through a regular week.

- If it's not looking so good, you need more support. It is available but you will need to ask.
- Talk to your doctor!

Tips to help...

- Get all the information on what you will need to do before you start treatment: How many tablets? How big are they? How often do you need to take them? How exact do you have to be with timing?
- Are there food or storage restrictions?
- Are there other choices?
- Use the daily chart in this leaflet to plan your timetable and use it to get used to the routine. For the first few weeks mark off each dose and the time that you took it.
- Make sure that you tell your hospital or clinic if you have difficulties with side effects. They can prescribe additional medication to help. They can also change the treatment if necessary.
- Divide up your drugs each morning or each week if you use a pill box if available. Then you can always check if you think you have missed a dose.
- Use a pill beeper if available or alarm watch. Use it for both morning and evening doses.
- Take extra drugs if you go away for a few days.
- Keep a small supply where you may need them in an emergency. This can be in a cool place at work or at a friend's house.
- Get friends to help you remember difficult dose times. Ask them to remind you when you are out socially.
- Ask friends who are already on treatment what they do. Ask them how well they are managing.
- Request your treatment center, clinic or hospital if they can arrange for you to talk to someone who is already taking the same treatment if you think this will help.
- Ask your doctor for a supply of medications to control nausea and diarrhoea. These side effects are the most common when starting therapy.
- Most combinations are twice-daily regimens. This usually means taking them every 12 hours. However, several drugs only need to be taken once a day. This usually means taking them every 24 hours.
- Completely missing a once-daily dose may be more serious than forgetting a dose from a twice-daily regimen.

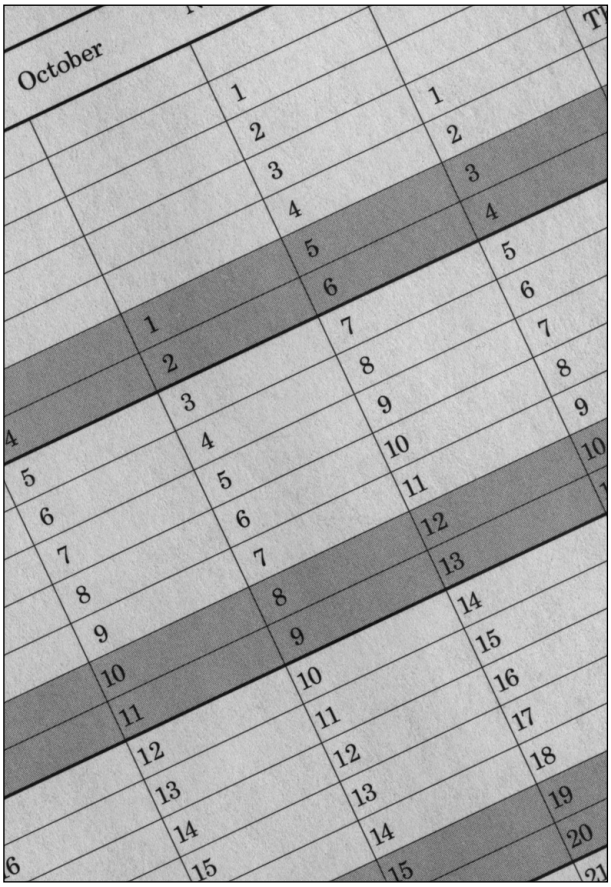
Adherence diary

Schedule planner: Use the top chart to plan your pill timetable with your doctor, nurse or pharmacist. Include medications for other illnesses or for side effects.

What if I forget to take my pills?

Almost everyone will forget or be late with their drugs at some time.

There is a difference though between occasionally missing a dose, and regularly forgetting on a daily or weekly basis. You need to aim to take all your doses at approximately the right time.



You may be regularly taking them late or missing doses completely. If this is the case it may be better to talk to your doctor about stopping treatment altogether.

This would at least limit your risk of resistance. You can restart treatment later when you are more able to cope with the regimen.

All these things are important in deciding which combination will suit you best.

You have to follow your regimen everyday. This includes both during the weekend, and in the different situations involved in life.

Taking days off your regimen is a very dangerous way of using treatment.

There are always things that can help you to avoid missing doses, whatever your lifestyle.

If you realise you have missed a dose; take it as soon as you remember. BUT, if you only realise when you're going to take your next dose, do not take a double dose.

Nutrition and HIV

Nutrition refers to how food is utilized by the body for growth, reproduction and maintenance of health.

Food contain different nutrients that include water, carbohydrates, proteins (or amino acids), lipids, vitamins and minerals.

Why is good nutrition important?

Good nutrition is essential for:

- Growth, development, replacement and repair of cells and tissues.
- Production of energy, warmth, movement and work.
- Carrying out chemical processes such as digestion, metabolism and maintenance.
- Protection against disease and recovery from disease.

Nutrients that are needed in large amounts, such as carbohydrates, proteins and fat are macronutrients. Vitamins and minerals which are needed in smaller amounts are micronutrients. Both macro and micronutrients are essential. They are needed in the right amounts and combinations for the body to function properly.

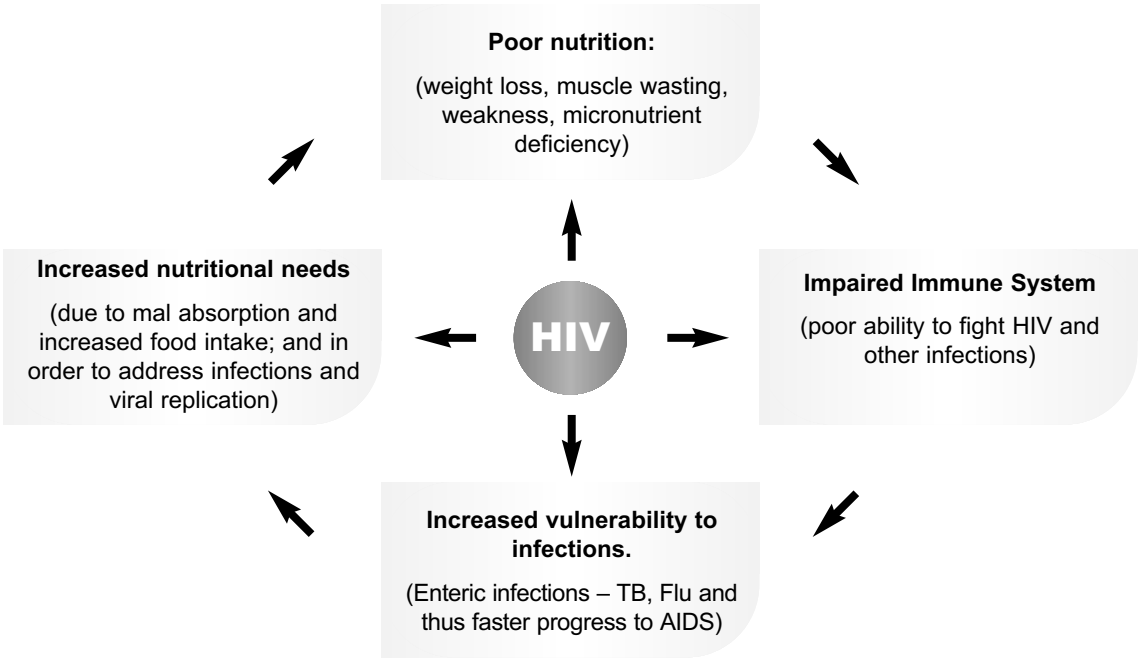
Food also needs to be free from infectious organism and harmful substances.

The link between nutrition and HIV/AIDS.

- The relationship between malnutrition and HIV/AIDS creates a vicious cycle that weakens the immune system.
- People with HIV/AIDS are at increased risk of malnutrition through various mechanisms, some of which are not related to food intake.
- Poor nutrition increases susceptibility to opportunistic infections and may accelerate the progression of HIV/AIDS.

“ good nutrition is essential for growth, development, replacement and repair of cells and tissues ”

The cycle of malnutrition and infection in the context of HIV/AIDS



Source: RCQHC/FANTA,2003

HIV impairs the Immune System making the body vulnerable to various infections. To handle the HIV infections and the frequent other illnesses the energy and nutrient needs are increased. If these increased needs are not met malnutrition results.

Malnutrition also contributes to the immune impairment, which worsens the effects of HIV and thus encourages more rapid progression to AIDS. Malnutrition therefore can both contribute to and result from the progress of HIV. Therefore good nutrition is important because it increases resistance to infection and disease, and improves energy, which makes a person stronger and more productive.

The increased risk of malnutrition in People Living With HIV / AIDS is due to:

- Reduced food intake as a result of appetite loss and difficulty eating. These may result from infections, side effects of medication or depression due to illness.

- Poor absorption of nutrients that may be due to recurrent / chronic diarrhoea and HIV causes intestinal damage.
- Changes in the way the body uses the nutrients it receives or has stored.
- Chronic infections and illness that accompany HIV that may increase the nutrient requirements of the body.

Good nutrition can therefore play an important role in the comprehensive management of HIV/AIDS, as it improves the immune system, boosts energy and helps recovers from opportunistic infections. ***Please make sure you see a dietician at your treatment center before starting medication.***

“good nutrition is important because it increases resistance to infection and disease”

Which combinations are best?

There isn't an answer to this question. This is because drugs that agree with one person can be more difficult to tolerate for another.

Although there are over 20 drugs that work against HIV, they are not all available in every country. This means that the best combination will vary depending on which drugs are available.

The combinations recommended in the WHO guidelines are discussed below and details of other drugs are given at the end of the booklet.

The best combinations will always include at least three different drugs, but often two three drugs are included in one pill. If you have access to only two drugs, and are already ill, then this will still work for a short time. If you use a combination with three drugs, it will last for much longer.

Any combination should preferably:

- Include three drugs
- Reduce your viral load to below detection – even if you do not have access to a viral load test to check this.
- Be a combination that you can tolerate, and include a schedule that you can follow, including any dietary restrictions.

Your doctor will discuss with you the drugs that are available and that are more likely to get your viral load undetectable. If you have taken HIV drugs before this will affect the choice. It will also affect how well your next treatment works.

Ask for information about dosing schedules, pill size and side effects so that you know what is involved for each combination.

Main drugs used

The most widely used drugs

NRTIs (Nucleoside Reverse Transcriptase Inhibitors):

d4T (stavudine)
3TC (lamivudine)
AZT (zidovudine)
ddI (didanosine)

NNRTIs (Non Nucleoside Reverse Trancriptase Inhibitors:

nevirapine
efavirenz

Other drugs that are used but are less widely available include:

NRTIs:

abacavir
tenofovir
FTC

PIs (Protease Inhibitors):

nelfinavir
indinavir
saquinavir
lopinavir/r (Kaletra)
atazanavir
fosamprenavir
ritonavir

Which combinations are recommended?

The World Health Organisation (WHO) guidelines in 2003 recommend one main combination for first-line therapy. This is the 'twice-daily' combination of:

- d4T (stavudine)
  +
- 3TC (lamivudine)
  +
- nevirapine

This is also the combination that is most widely available.

Each of these drugs is available individually from several manufacturers and all three drugs are available in one pill called a Fixed Dose Combination (FDC). Triomune from Cipla and Triviro from Ranbaxy are FDCs that were first approved by the WHO and other formulations from other companies are likely to be approved over the next year.

In 2004 some of these drugs were temporarily withdrawn, but they should be resubmitted in late 2004 and early 2005. The active content of these drugs is still expected to be the same as brand name drugs.

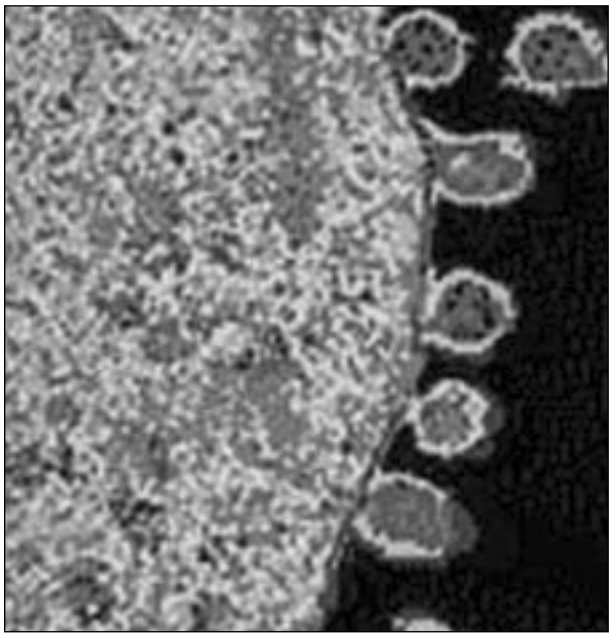
If you weigh less than 60kg, or if you develop neuropathy or other side effects linked to d4T then you should only use a 30mg rather than 40mg dose of d4T.

Both FDCs are available with d4T dosed at either 30mg or 40mg doses. You need check to see which dose you are using. A lower dose of 20mg may also be effective if you have no other choices and you are still getting side effects.

- AZT (zidovudine) can be used instead of d4T, although the Fixed Dose Combination for AZT + 3TC + nevirapine had not been approved by the WHO when this booklet was printed.

- Efavirenz can be used instead of nevirapine, with either d4T + 3TC or AZT + 3TC and is recommended when TB medication is also needed. Efavirenz should not be taken by pregnant women.

- AZT and d4T should NEVER be used in the same combination.



The different side effects linked to each of these main drugs are discussed in Section 4. Side effects are a common reason to change from one drug to another.

Protease inhibitors are not recommended in the WHO guidelines because they are generally much more expensive and involve more pills. This family of drugs is discussed in more detail in Section 9.

Do generic drugs work?

Generic drugs are just as good as non-generic drugs.

They have exactly the same amount of active ingredients.

They are manufactured in several countries including India, Brazil, Thailand and South Africa. The lower cost of manufacturing in these countries is one of the reasons that they can be produced at a lower cost, and this means that more people can be treated for the same money.

These drugs are just as effective as non-generic drugs, and every country in the world uses generic drugs to treat different illnesses, especially Western countries in Europe and America.

What about side effects?

Everyone worries about side effects from any medicine. But most people find that, within a few weeks of starting HIV treatment, side effects reduce and therapy becomes an ordinary and manageable part of daily life.

- Most side effects are usually mild.
- They can often be reduced with other medication that is easy to use.
- There is a small risk of more serious side effects, but these should be picked up by routine monitoring from your doctor. More information about these side effects is included below.

Ask your doctor, nurse or HIV pharmacist about the side effects related to the drugs that you use. Ask how likely they are to occur. Ask how many people stop treatment because of them (usually very few). Even rough estimates will give you a good idea of what is involved.

Nausea (feeling sick), diarrhoea and tiredness are the most common general side effects. These often become easier after the first few weeks. Very rarely, nausea and tiredness can be very serious. This is why you should tell your doctor of any problems.

Ask your doctor or pharmacist for anti-nausea and diarrhoea medications when you first start therapy so you can use these if you need them. If these medications aren't effective, ask your clinic for stronger or more effective drugs.

More serious side effects

Liver toxicity: nevirapine, efavirenz

Although liver toxicity with nevirapine (or efavirenz) is not very common it can be very serious and life-threatening if it does occur. Less than 5% people have to change treatment for this reason, but because nevirapine is included in Fixed Dose Combinations (FDCs) it is very important to know about these symptoms.

If you have a rash with nevirapine, it is important that you have a blood test to check whether your liver is being affected (called Liver Function Tests or LFTs).

If this is not available, other symptoms include:

- Feeling sick (nausea) or being sick (vomiting)
- Poor appetite
- If your eyes or skin looks more yellow
- Light coloured stool or dark coloured urine
- Tenderness or swelling in your liver - you liver is just below your stomach

If you have any of these symptoms, you should contact your doctor straight away.

Liver toxicity usually occurs in the first 6 weeks of treatment, but can also occur later. If you are coinfected with hepatitis then the risk of liver toxicity is much higher, and another choice of drug would be more appropriate.

Rash: nevirapine

About 10-15% people who use nevirapine or efavirenz get a low level rash that is not serious, and about 5% people discontinue the drug because of this.

However, 2-3% people can be at risk of a much more serious rash, especially using nevirapine.

Nevirapine should be given at a reduced dose for the first two weeks that it is used, but this does not always happen with Fixed Dose Combinations.

The nevirapine dose should NEVER be increased if you still have a rash.

If the rash covers more than 10% of your body or breaks the skin at all, you must see your doctor immediately. In these rare cases, nevirapine has to be stopped very quickly to reduce the risk of a severe reaction that can be fatal.

Peripheral neuropathy: d4T, rarely 3TC

Peripheral neuropathy is the term for damage to the nerves in your hands or feet. Sometimes this starts as a tingling or numbness, but if it is allowed to develop it can become very painful and permanent and move up your limbs.

Although it is sometimes caused by HIV, it can also be a side effect from some HIV drugs. It is also more likely if you start treatment with a very low CD4 count. The main drugs linked to neuropathy are ddC (which is rarely used), d4T, ddI and to a lesser extent, 3TC.

d4T is one of the drugs in Triomune, and d4T is currently recommended in first-line therapy in many countries.

This means that you have to be very aware of any tingling or pain in your hands or feet and report this to your doctor.

Because there is no cure for neuropathy, the best choice is to stop using d4T and change it to another drug.

Many people are also able to reduce the dose of just the d4T part of your combination. Triomune for example comes with a dose of either 30mg or 40mg of d4T. If you can get each drug prescribed separately, then you may be able to reduce to dose even further to 20mg twice a day.

If there are no other treatment choices, and you are otherwise doing well, then it may be better to stop your treatment for a period until there are new treatment choices.

Neuropathy can reverse by itself when you stop the drug that is causing it, but only if you stop the drug before serious damage has been caused. You and your doctor should manage this important side effect very carefully.

Lipodystrophy: d4T, AZT, nevirapine, efavirenz, protease inhibitors

Lipodystrophy refers to changes in fat cells and the distribution of body fat. This can result in losing fat from your arms, legs and face or gaining fat around your stomach, breasts or shoulders. It also includes changes in blood fat and blood sugar levels.

Different drugs may be responsible for fat gain and fat loss. Fat accumulation, to the stomach or breasts and/or across the shoulders, has been more linked to protease inhibitors and NNRTIs. Fat loss, from arms, legs, face and buttocks, has been linked mainly to d4T, and to a lesser extent to AZT.

d4T and AZT are both drugs that are included in recommended first line therapy in the WHO guidelines.

We do not know what causes lipodystrophy. Symptoms can occur rarely in HIV-positive people who are not on treatment. Lipodystrophy usually, but not always, develops slowly over many months or years.

Early symptoms may reverse if you switch to different HIV drugs. Exercise and dietary changes can also help. Careful body measurements by a dietician, by DEXA scan, or photographs can monitor changes. These tests may not be available in your country.

Regular blood tests will check for other side effects. If you have any difficulties, make sure your doctor takes them seriously and does something about it.

Anaemia: AZT

Anaemia is a shortage of oxygen-carrying red blood cells whose symptoms are extreme tiredness, and it is caused by AZTs effect on bone marrow.

Lower doses of AZT may be just as effective against HIV, but this is not possible in the currently available Fixed Dose Combinations.

If you are using AZT and become extremely tired or weak, you need to see your doctor who should perform a blood test or change this treatment.

Lactic acidosis: d4T, ddI, AZT

Lactic acidosis is a term for a dangerous build up of lactate in the blood. The symptoms include feeling sick and/or very tired and muscle weakness. The risk of lactic acidosis is much higher when d4T is used with ddI - and these two drugs are not recommended to be used together in most guidelines.

If you have these symptoms, it is essential to contact your doctor.

Mood changes, strange dreams, nervousness: efavirenz

Efavirenz is linked to one set of side effects that are different to all the other drugs. This is because it can affect your mood and feelings. You may feel disorientated or anxious when you start taking efavirenz and you may have vivid or disturbing dreams. This is a side effect of this drug.

Most people get some changes when they first start to take efavirenz, but this also reduces after the first few weeks, and is much easier to manage.

However, some people get very serious problems and should contact their doctor to switch to another drug. Efavirenz can make your worries or depression worse and you need to be aware of this if you start a combination that includes this drug.

Other side effects

This booklet has focused on the more serious side effects that also occur more rarely. However anything that makes you feel unwell - even if they are not classed as serious is something you should tell your doctor about.

Can I change treatments?

If your first combination is too difficult to follow, or if any initial side effects have not improved after the first few weeks or months then there may be an alternative drug or combination that you can change to.

If this is your first combination, you have more choice. You should not put up with difficult side effects for months on end.

Can I take a break in my treatment?

Once you start treatment, it is best not to take any break or interruption unless your doctor recommends this.

To benefit from HIV treatment you need to take every dose on time for at least six months. Even after this the longer you stay on treatment the longer the benefit should continue.

If you get a very good response to treatment and start to feel better, it is still important to continue taking every dose of treatment on time.

- Stopping treatment for any short period is therefore not recommended. Levels of HIV in your blood - your viral load - can increase again very quickly (from undetectable to several thousand in a few weeks). Each interruption of treatment also carries a risk of developing drug resistance.
- An interruption may be reasonable if you have a very strong CD4 count or have very difficult side effects.
- If you want to take a treatment break, it is essential you talk to your doctor first. Some drugs have to be stopped all together, and others need to be stopped at different times.

Recreational drugs, alcohol and complementary therapy

Some HIV drugs interact with recreational drugs, street drugs, methadone and complementary or traditional herbal therapies.

The interactions can be complicated and involve both higher and lower exposure to HIV or other drugs.

It is therefore very important that your HIV doctor and pharmacist know about any other drugs or supplements that you use. Even if you use them rarely. Your doctor will treat this information in confidence.

Alcohol does not interact with HIV medications. However, heavy alcohol use, as with recreational drug use, may reduce adherence. It would help if your healthcare workers know about this.

Table 1: Serious side effects from main WHO drugs

Drug Name	Side effcts	Symptoms
d4t (stavudine)	Peripheral neuropathy (PN)	Loss of feeling (numbness) OR pain in fingers and/or toes
	Lactic acidosis	**Feeling sick, vomiting, no appetite, extreme tiredness**
	Lipoatrophy	Loss of fat in face, arms, legs or buttocks. Veins become more prominent
3TC (lamivudine)	Hair loss (rare)	Hair thinning or falling out
	PN (rare)	Loss of feeling (numbness) OR pain in fingers and/or toes
AZT (zidovudine)	**Anaemia**	**Feeling tired or weak**
	Lipoatrophy	Loss of fat in face, arms, legs or buttocks. Veins become more prominent.
nevirapine	**Liver toxicity**	**Feeling sick, vomiting, poor appetite, yellow eyes or skin, light coloured stool or dark coloured urine, tenderness or swelling in your liver**
	Rash	**Redness or small rash on skin**
	Severe rash	**Any rash over more than 10% of body, any broken skin**

Table 1 contd

efavirenz	CNS side effects	Mood changes, feeling disorientated or anxious, vivid or disturbing dreams, change in sleep pattern. If severe then urgent to see doctor.
	Liver toxicity	**Feeling sick, vomiting, poor appetite, yellow eyes or skin, light coloured stool or dark coloured urine, tenderness or swelling in your liver**
	Rash	**Redness or small rash on skin**
	Severe rash	**Any rash over more than 10% of body, any broken skin**

Resistance

What is resistance?

This section has been left almost to the end, but it is very important. It is also the reason that all through the booklet we talk about perfect adherence.

Resistance to anti-HIV drugs occurs when the structure of the virus makes tiny changes called mutations. If these changes are made when you are on treatment, it can mean that the drugs will no longer work.

You can also be infected with a strain of HIV that is already resistant to some or all HIV drugs. Some countries have tests for resistance but in others, they are either very expensive or not available at all.

How does resistance occur?

Mutations that lead to drug resistance are generally only produced when you continue taking a treatment with a detectable viral load. This is most likely to happen if you miss doses of your drugs or take them late.

Whenever the level of a drug falls below a certain minimum level, you are at risk of developing resistance

If you are monitored with a viral load test and your viral load is detectable when on treatment, this can be an early indication that your treatment is not working so well and that you may develop resistance.

What is cross-resistance?

Some drugs are cross-resistant to others. This means that if you become resistant to one drug you will also be resistant to other similar drugs, even if you have never taken them before. This is particularly true of drugs in the same class.

There are also varying degrees of cross-resistance.

Sometimes you may still get some benefit from the second drug but the response is less likely to be as strong.

How do I avoid resistance?

Avoiding resistance is one of the most important conditions for using combination therapy. You need to use a combination that is potent enough to minimise the risk of getting resistance to any of the drugs you take.

The best chance you have of stopping resistance involves reaching and maintaining undetectable on viral load tests that measure down to 50 copies/ml.

So little HIV is produced at this level that resistance is unlikely to develop to your combination. So long as you continue taking the drugs carefully, you could use them for many years.

Which drugs, which combination?

Main kinds of HIV drugs:

- **RTI**: 'reverse transcriptase inhibitor' also called nucleoside or nucleotide analogue or 'nukes'
- **NNRTI**: 'non-nucleoside reverse transcriptase inhibitor' or 'non-nukes'
- **PI:** 'protease inhibitor'
- **FI**: 'fusion inhibitor'

The strategy for using HIV drugs has been consistent for the last five years.

The main principle is that any combination needs to include at least three drugs. Using only one or two drugs in a combination is likely to lead to resistance.

Combinations usually include drugs from two different families. This involves choosing two 'nukes', plus either an NNRTI or a protease inhibitor, or more recently a boosted protease inhibitor.

The best results from clinical trials have been using combinations based on this formula. This is reflected in WHO and other treatment guidelines.

The WHO guidelines recommend the third drug to be an NNRTI. This is mainly because they require fewer pills or diet requirements.

Which nukes?

There are currently six main RTIs ('nukes') to use in first-line therapy. These are d4T, AZT, 3TC, FTC, abacavir, ddI and tenofovir. FTC is a new drug similar to 3TC but it is less widely available. Some of these drugs are not yet available in generic formulations.

Although d4T is widely used, it is linked to peripheral neuropathy and to lipoatrophy (fat loss). Another RTI, ddC, is licensed, but rarely used because of side effects.

Most combinations of two of these drugs are used but a few cannot be. For example, you should never use AZT and d4T in the same combination because they cancel each other out. 3TC and FTC cannot be used together either.

d4T and ddI should not be used together because the risk of serious side effects increases - especially during pregnancy.

Each drug and combination will have specific advantages and disadvantages. They will have different dosing regimens and side effects.

More importantly, unless there is an interaction, most nukes are interchangeable. This means that if you get side effects with one drug you can switch to another.

Which NNRTI – efavirenz or nevirapine?

Most doctors think there is little difference in anti-HIV activity between these two drugs. Both these drugs have some similar side effects. This includes risk of rash and liver toxicity, which can be serious and occasionally fatal. Careful monitoring will check for this.

The main differences are:

- Nevirapine cannot be used if you are using rifamycin to treat TB
- Nevirapine can cause a serious allergic reaction called Stevens-Johnson Syndrome (SJS) in less than 1% of people and can cause fatal liver failure.
- Nevirapine should not be used by women if they have a CD4 count over 250 when they start treatment

The reactions with nevirapine usually only occur in the first two months of treatment. Over this time, you should be monitoring every two weeks. Otherwise, nevirapine is an easy drug to tolerate.

The main side effects of efavirenz relate to the Central Nervous System (CNS). They include mood changes, anxiety, depression and sleep disturbance that includes vivid dreams and nightmares.

They occur in more than half the people who first use efavirenz and usually reduce after a few days or weeks. About 3% of people stop efavirenz because they get severe CNS symptoms. About 10-15% of people may stop later because of the effect on their quality of life.

Efavirenz can also cause liver toxicity and rash, although less often than nevirapine.

Protease inhibitors

If you are not using an NNRTI as the third drug, you should use a protease inhibitor preferably boosted by ritonavir.

This includes lopinavir/r (Kaletra), which has ritonavir inside the capsule. It also includes indinavir, saquinavir, atazanavir or fosamprenavir, which can all be boosted with a separate ritonavir pill or pills taken at the same time.

“the main principle is that any combination needs to include at least three drugs. Using only one or two drugs in a combination is likely to lead to resistance”

Using a small dose of ritonavir in these combinations provides higher and more stable drug levels. This reduces the risk of resistance. It also reduces the numbers of pills and dietary requirements compared to unboosted PIs. Some people though find even small doses of ritonavir increase nausea.

Choice or protease inhibitor will depend on which drugs are available in your country. Many PIs become stronger when used with small doses of ritonavir and in many countries they are always recommended to be used this way.

Whether you use NNRTI or PI-based regimens will depend on discussions with your doctor, the choices of drugs available, your previous health and whether you have any prior drug resistance.

Triple nucleoside combinations

Combinations with three 'nukes' are less effective as first-line treatment. This is not a recommended first choice combination in treatment guidelines.

Although a combination with only 'nukes' is not recommended for starting treatment, you may be able to cut down to a 'nuke'-only combination. This is usually after a successful response to PI or NNRTI-containing treatment.

The main reason to try this would be to reduce side effects related to PIs or NNRTIs. This includes increased blood lipids or fat accumulation (lipodystrophy).

New non-standard approaches

Using two 'nukes' plus either an NNRTI or a boosted PI has produced the most effective, durable and tolerable results for combination therapy.

Recent trials are looking at other approaches. So far, however, they have not produced the same success.

For example, some studies do not use 'nukes' at all. By using either dual-boosted PIs (and in one case single-boosted PI), or PI+NNRTI combinations, they hope to avoid some of the side effects associated with 'nukes'.

However, not all 'nukes' have similar side effects. This is especially true for the link to lipoatrophy and fat loss. It may therefore be better to choose from abacavir, tenofovir, 3TC and FTC, rather than cut out 'nukes' altogether.

Also, many people do not get side effects on these drugs. It may again be better to see whether this is an issue before breaking from the recommended combinations.

Drugs and doses

The following table is a reference for different names of drugs, dosing, total pill count and brief details of food restrictions. Alternative doses are required for some combinations. Some drugs (ritonavir, nevirapine) start at lower doses for the first 1 or 2 weeks.

Name, Brand & other names	Dosing	Total daily pills	Food restrictions
REVERSE TRANSCRIPTASE INHIBITORS (RTIs)			
d4T, Zerit, stavudine	1 capsule, twice daily	2	none
AZT, Retrovir, zidovudine	1 capsule, twice daily	2	none
ddI Videx, didanosine, 100mg	4 tablets, once daily	4	do not eat for 2 hours before and I hour after (2 hours after for EC)
200mg 'Reduced mass' ddI	2 tablets, once daily	2	
ddI/EC 'Enteric coated' formula	1 capsule, once daily	1	take on empty stomach
3TC (150mg) Epivir, lamivudine	1 tablet, twice daily	2	none
3TC (300mg) Epivir, lamivudine	1 tablet, once daily	1	none
abacavir, Ziagen	1 tablet, twice 2 daily	2	none
tenofovir, Viread	1 tablet, once daily	1	take with food
FTC. emtracitabine	1 capsule, once daily	1	none
Multi-nuke FDCs			
AZT+3TC together (i.e. Combivir)	1 tablet, twice daily	2	none
AZT+3TC+abacavir (ie Trizivir)	1 tablet, twice daily	2	none

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)

efavirenz, Sustiva	1 x 600mg tablet once daily	1	not with high-fat meal
	OR		
	3 x 200mg capsules, once daily	3	not with high-fat meal
nevirapine, Viramune	1 tablet, twice daily	2	none

DUAL & BOOSTED PROTEASE COMBINATIONS [the most used doses]

lopinavir/r, Kaletra	3 capsules, twice daily	6	take with food
indinavir/ritonavir	400mg/400mg, 1xIDV / 4xRTV twice daily,	1 0	None
	800mg/200mg, 2xIDV / 2xRTV, twice daily,	8	None
	800mg/100m, 2xIDV / 1xRTV, twice daily	6	None
saquinavir/ritonavir [Invirase, hard gel formulation of saquinavir can be used instead of Fortovase soft gel capsule when using ritonavir. Invirase is a smaller pill with less side effects]	400mg/400mg, 2xSQV / 4xRTV, twice daily ,	1 2	food reduces side effects,
	1000mg/100mg, 5xSQV / 1xRTV, twice daily	1 2	food reduces side effects
atazanavir*/ritonavir	300mg/100mg2xATV/ 1 x RTV, once daily	3	None

fosamprenavir*/ ritonavir	700mg/100mg 1xFosAPV /1xRTV, once or twice daily	1 or 2	None
SINGLE PROTEASE INHIBITORS (PIs)			
indinavir, Crixivan	2 capsules, 3 times daily	6	2 hrs after food and 1 hr before
nelfinavir, Viracept (film coated)	5 tablets, twice daily	10	take with meal
atazanavir, Reyataz	2 capsules, once daily	2	take with meal
ENTRY INHIBITORS (Fusion inhibitors)			
enfuvirtide, T-20, Fuzeon	subcutaneous injection, twice daily		None

Feedback form

Name	
Position in Organisation	
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Questions:	
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Qn2: Does it meet your treatment knowledge needs?	
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